

zoetis

KETOFEN® (ketoprofen)

Injectable Solution, 100 mg/mL



For subcutaneous use in certain classes of cattle.
See INDICATIONS below.

CAUTION

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION

Ketoprofen is a non-steroidal anti-inflammatory agent of the propionic acid class that includes ibuprofen, naproxen, and fenoprofen. **Active Ingredient:** Each mL contains 100 mg ketoprofen/mL of aqueous solution. **Inactive Ingredients:** 70 mg L-Arginine/mL; citric acid (to adjust pH); benzyl alcohol, 0.025 g (as preservative).

It is packaged in a multiple dose bottle.

INDICATIONS

KETOFEN® (ketoprofen) is indicated for the control of pyrexia associated with Bovine Respiratory Disease (BRD) in beef heifers, beef steers, beef calves 2 months of age and older, beef bulls, replacement dairy heifers, and dairy bulls. Not for use in reproducing animals over one year of age, dairy calves, or veal calves. Not for use in lactating dairy cattle or calves <2 months old.

DOSAGE AND ADMINISTRATION

Cattle: The recommended dosage is 3 mg/kg (1 mL/33.3 kg) or 1.36 mg/lb (1 mL/74 lb) of body weight. Treatment is administered by subcutaneous injection once daily and may be repeated for up to three days if pyrexia persists.

Use contents within 4 months of first vial puncture.

Cattle Dosing Guide:

Animal Weight (lb)	Dose Volume (mL)	Animal Weight (lb)	Dose Volume (mL)
150	2.1	600	8.4
200	2.8	650	9.1
250	3.5	700	9.8
300	4.2	750	10.5
350	4.9	800	11.2
400	5.6	850	11.9
450	6.3	900	12.6
500	7.0	950	13.3
550	7.7	1000	14.0

CONTRAINDICATIONS

Do not use in animals showing hypersensitivity to ketoprofen.

WITHDRAWAL PERIODS AND RESIDUE WARNINGS

Cattle must not be slaughtered for human consumption within 48-hours following last treatment with this drug product. Not for use in female dairy cattle 1 year of age or older, including dry dairy cows; use in these cattle may cause drug residues in milk and/or in calves born to these cows or heifers. Not for use in beef calves less than 2 months of age, dairy calves, and veal calves. A withdrawal period has not been established for this product in pre-ruminating calves.

USER SAFETY WARNINGS

Not for human use. Keep this and all drugs out of the reach of children.

The Safety Data Sheet (SDS) provides more detailed occupational safety information. To obtain a Safety Data Sheet contact Zoetis Inc. at 1-888-963-8471.

ANIMAL SAFETY WARNINGS

Do not use in cattle that are dehydrated or with known renal disease.

PRECAUTIONS

As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal, hepatic and renal toxicity. Sensitivity to drug-associated adverse effects varies with the individual patient. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with renal, cardiovascular, and/or hepatic dysfunction.

Since many NSAIDs possess the potential to induce gastrointestinal ulceration, concomitant use of KETOFEN® with other anti-inflammatory drugs, such as other NSAIDs and corticosteroids, should be avoided or closely monitored. Discontinue use if fecal blood is observed.

The effects of KETOFEN® on bovine reproductive performance, pregnancy, lactation, or on animals of reproductive age intended for breeding has not been investigated.

KETOFEN® may cause injection site swelling that appears 1 to 3 days post-treatment and typically resolves by 28 days post-injection. These reactions may result in trim loss of edible tissue at slaughter.

ADVERSE REACTIONS

Repeated administration of NSAIDs can result in gastric or renal toxicity. Sensitivity to drug-associated adverse effects varies with the individual patient. Patients at greatest risk for toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with pre-existing gastric ulcers, renal, cardiovascular, and/or hepatic dysfunction.

CONTACT INFORMATION

For a copy of the Safety Data Sheet or to report suspected adverse drug experiences, call Zoetis Inc. at 1-888-963-8471. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae.

CLINICAL PHARMACOLOGY

KETOFEN is a non-narcotic, non-steroidal anti-inflammatory agent. The primary mechanism of action for ketoprofen is inhibition of the cyclooxygenase (COX) pathway leading to decreased production of prostaglandins^[1]. Ketoprofen is a relatively nonselective inhibitor of the COX isozymes. After subcutaneous administration of a single dose of 3 mg/kg ketoprofen in fourteen calves, the mean and range (minimum and maximum) for the maximum plasma concentration (C_{max}) was 9.40 µg/mL (7.06 – 15.8), the area under the curve to the last quantifiable point AUC_(last) was 67.4 µg·h/mL (48.4 – 96.9), the time to maximum plasma concentration (T_{max}) was 1.54 hours (0.67-2.0), and the half-life (t_{1/2}) was 3.03 hours (2.48-3.88). Ketoprofen has shown linear pharmacokinetics across a 1 to 15 mg/kg dose range and has shown little to no accumulation on multiple dosing with a 24-hour dose interval.

EFFECTIVENESS

The control of pyrexia associated with bovine respiratory disease (BRD) was demonstrated in a single multisite study. Cattle exhibiting clinical signs of BRD and having a rectal temperature of at least 104.5°F were enrolled. A total of 202 cattle were administered either a single subcutaneous injection of KETOFEN® (3.0 mg/kg BW) or a single subcutaneous injection of saline (0.028 mL/kg BW) on day 0. Six hours after treatment, rectal temperatures were measured. The treatment success rate of the KETOFEN®-treated group was compared to the treatment success rate in the saline-treated group. A treatment success was defined as a decrease in rectal temperature of ≥ 2°F in an individual animal. The percent of animals with a ≥ 2 degree decrease in rectal temperature at 6 hours post-treatment was significantly different and higher (P=0.0215) in the KETOFEN® group (74.3%) vs. the saline treated group (5.9%).

TARGET ANIMAL SAFETY

Margin of Safety: KETOFEN® was injected with a 1X (3 mg/kg BW), 3X (9 mg/kg BW), and 5X (15 mg/kg BW) dose daily for 9 consecutive days (3 times the maximum recommended duration). The only treatment-associated finding present at a 1X (3 mg/kg BW) dose for 9 days was minimal to mild gross and microscopic renal tubular lesions. No ketoprofen-related changes were noted in clinical or general health observations, hematology, urinalysis, fecal occult blood, or serum chemistries in cattle administered a 1X (3 mg/kg BW) dose for 9 days. At a 3X dose, subclinical focal ulcers in the abomasum and minimal to mild renal lesions were present. Cattle injected with a 5X dose of ketoprofen for 9 days had similar treatment related findings, except for one of eight calves which had clinical signs of toxicity, due to peritonitis subsequent to abomasal ulceration on the 9th treatment day. Discontinue treatment if fecal blood is observed. Do not use in cattle that are dehydrated or with known renal disease.

Injection site safety: Eight calves were injected with a 1X dose of ketoprofen daily for 3 consecutive days with clinical observations of injection sites with necropsy on days 7, 14, 28, and 42. Injection of 3 consecutive doses of KETOFEN® resulted in transient injection site reactions palpable through 14 days, with resolution by 28 days post-administration. Injection site lesions included discoloration involving the skin and subcutaneous tissue on Day 7. By Day 42 discoloration was limited to subcutaneous tissue. Subcutaneous injection of ketoprofen can cause a transient local tissue reaction. These reactions may result in trim loss of edible tissue at slaughter.

Field safety: There were no adverse events reported in investigational field studies with the injection of KETOFEN® under the intended conditions of use.

REFERENCES

1. Paresch B, R.S., RD Varia, JH Patel, UD Patel, SK Bhavsar and AM Thaker, *Impact of multiple intravenous administrations of ketoprofen on blood profile in cow calves*. Inter J Vet Sci, 2012. 1(1): p. 34-36.

HOW SUPPLIED

KETOFEN® (ketoprofen) 100 mg/mL is available in 50 mL and 100 mL multidose bottles.

STORAGE CONDITIONS

Store below 25°C (77°F), with brief excursions permitted between 0°C - 40°C (32°F - 104°F).

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Zoetis Manufacturing and Research Spain, S.L.
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